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NEWS 3 Feb 06 Engineering Information Encompass files have new names
NEWS 4 Feb 16 TOXLINE no longer being updated
NEWS 5 Apr 23 Search Derwent WPINDEX by chemical structure
NEWS 6 Apr 23 PRE-1967 REFERENCES NOW SEARCHABLE IN CAPLUS AND CA
NEWS 7 May 07 DGENE Reload
NEWS 8 Jun 20 Published patent applications (A1) are now in USPATFULL
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NEWS 10 Aug 23 In-process records and more frequent updates now in
MEDLINE
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NEWS 13 Sep 17 IMSworld Pharmaceutical Company Directory name change
to PHARMASEARCH
NEWS 14 Oct 09 Korean abstracts now included in Derwent World Patents
Index
NEWS 15 Oct 09 Number of Derwent World Patents Index updates increased
NEWS 16 Oct 15 Calculated properties now in the REGISTRY/ZREGISTRY File
NEWS 17 Oct 22 Over 1 million reactions added to CASREACT
NEWS 18 Oct 22 DGENE GETSIM has been improved
NEWS 19 Oct 29 AAASD no longer available
NEWS 20 Nov 19 New Search Capabilities USPATFULL and USPAT2
NEWS 21 Nov 19 TOXCENTER(SM) - new toxicology file now available on STN
NEWS 22 Nov 29 COPPERLIT now available on STN
NEWS 23 Nov 29 DWPI revisions to NTIS and US Provisional Numbers
NEWS 24 Nov 30 Files VETU and VETB to have open access
NEWS 25 Dec 10 WPINDEX/WPIDS/WPIX New and Revised Manual Codes for 2002
NEWS 26 Dec 10 DGENE BLAST Homology Search

NEWS EXPRESS August 15 CURRENT WINDOWS VERSION IS V6.0c,
CURRENT MACINTOSH VERSION IS V6.0 (ENG) AND V6.0J (JP),
AND CURRENT DISCOVER FILE IS DATED 07 AUGUST 2001

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FILE 'USPATFULL' ENTERED AT 12:06:52 ON 13 DEC 2001
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=> s fenofibrate
L1 2786 FENOFIBRATE

=> s soybean oil and coconut oil or canola oil or corn oil or palm oil or cottonseed oil or olive oil or peanut oil or safflower oil or sesame oil
L2 94973 SOYBEAN OIL AND COCONUT OIL OR CANOLA OIL OR CORN OIL OR PALM OIL OR COTTONSEED OIL OR OLIVE OIL OR PEANUT OIL OR SAFFLOWER OIL OR SESAME OIL

=> s emulsifier or emulsion or sorbitan fatty acid or castor oil or ethoxylate
L3 419779 EMULSIFIER OR EMULSION OR SORBITAN FATTY ACID OR CASTOR OIL OR
ETHOXYLATE

=> s 11 and 12 and 13
L4 67 L1 AND L2 AND L3

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=> s 14 and py<1999  
1 FILES SEARCHED...  
3 FILES SEARCHED...  
15          6 14 AND
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=> dup rem 15
PROCESSING COMPLETED FOR L5
L6          6 DUP REM L5 (0 DUPLICATES REMOVED)
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=> d 16 1-6 ab bib kwic

L6 ANSWER 1 OF 6 USPATFULL
AB A method for preventing or treating high serum levels of cholesterol
and

lipids in a mammal, said method comprising orally administering an effective amount of natural lycopene to prevent or treat high serum levels of cholesterol or lipids to a mammal in need of such treatment. Also disclosed is an oral pharmaceutical composition in unit dosage form for oral administration for the prevention or treatment of high serum

levels of cholesterol and/or lipids in a mammal, said composition comprising an effective amount of natural lycopene to prevent or treat high serum levels of cholesterol or lipids in a mammal and in a sufficient amount to achieve a level of serum cholesterol of less than 200 mg per deciliter over the course of treatment, and a pharmaceutically acceptable carrier therefor.

AN 2001:112374 USPATFULL
TI Methods of preventing and/or treating high serum levels of cholesterol and/or lipids
IN Clark, James P., Naperville, IL, United States
Dunker, Manfred S., Palos Park, IL, United States
PA Henkel Corporation, Gulph Mills, PA, United States (U.S. corporation)
PI US 6262109 B1 20010717
WO 9619217 19960627 <--
AI US 1997-849977 19970822 (8)
WO 1995-US16774 19951222
19970822 PCT 371 date
19970822 PCT 102(e) date

DT Utility
FS GRANTED

EXNAM Primary Examiner: Criares, Theodore J.
LREP Drach, John E., Murphy, Glenn J., Ettelman, Aaron R.
CLMN Number of Claims: 7
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 330

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
PI US 6262109 B1 20010717
WO 9619217 19960627 <--

SUMM The drugs which are being used in these studies are, for example, clofibrate, gemfibrozil, **fenofibrate** and bezafibrate or a combination of cholestyramine and niacin. These reports clearly support the theory that lowering of serum cholesterol. . .

SUMM . . . natural tocopherol, especially alpha-tocopherol, with or without natural beta-carotene. The natural beta-carotene is preferably obtained from natural sources, such as **palm oil** or algae.

SUMM . . . natural tocopherols are derived from vegetable oils. Soy oil is the most widely used source. Sunflower, corn, peanut, rapeseed and **cottonseed oils** may also be used. Natural tocotrienol and natural tocopherols are very different from that produced by chemical synthesis, i.e., synthetic. . .

SUMM . . . carrier. Thus, for example, when administered orally, the active ingredient is formulated in the form of soft gelatin capsule, elixir, **emulsion** and the like employing methods well known in the art. Suitable formulations and formulation techniques can be found in Remington's. . .

DETD About 5 mg units of lycopene is mixed in a suitable blender with about 450 mg of **peanut oil**. It is then dispensed in the form of soft gelatin capsule.

L6 ANSWER 2 OF 6 USPATFULL

AB The present invention relates to novel tocotrienols and tocotrienol-like compounds displaying biological activity. The tocotrienols and tocotrienol-like compounds of this invention may be conveniently obtained from biological sources or by chemical synthesis and may be used in pharmaceutical compositions, foodstuffs and dietary supplements.

This invention also relates to the use of tocotrienols, tocotrienol-like compounds, and mixtures thereof, as hypocholesterolemic, antithrombotic, antioxidantizing, antiatherogenic, antiinflammatory and immunoregulatory agents, or as agents useful to decrease lipoprotein (a) concentration in

the blood or to increase feed conversion efficiency.

AN 1998:124588 USPATFULL
TI Tocotrienols and tocotrienol-like compounds and methods for their use
IN Lane, Ronald H., Phoenix, AZ, United States
Qureshi, Asaf A., Madison, WI, United States
Salser, Winston A., Pacific Palisades, CA, United States
PA LipoGenics, Inc., Scottsdale, AZ, United States (U.S. corporation)
PI US 5821264 19981013 <--
AI US 1996-719284 19960924 (8)
RLI Continuation of Ser. No. US 1994-244215, filed on 15 Aug 1994, now patented, Pat. No. US 5591772 which is a continuation-in-part of Ser. No. US 1991-796486, filed on 22 Nov 1991, now abandoned

DT Utility

FS Granted

EXNAM Primary Examiner: Raymond, Richard L.

LREP Lyon & Lyon LLP

CLMN Number of Claims: 32

ECL Exemplary Claim: 1

DRWN 14 Drawing Figure(s); 13 Drawing Page(s)

LN.CNT 3191

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

PI US 5821264 19981013 <--
SUMM . . . ("T"). Tocotrienols and tocopherols occur naturally in small quantities in a wide variety of plant sources, such as rice bran, **palm oil** and barley (A. A. Qureshi et al., "Lowering of Serum Cholesterol in Hypercholesterolemic Humans by Tocotrienols (Palmvitee)", Am. J. Clin.. . .

SUMM . . . al. (1986), supra. Various human and animal studies have confirmed the impact of pure tocotrienols, isolated from barley, oats and **palm oil**, on cholesterol biosynthesis, specifically LDL-cholesterol (A. A. Qureshi et al., "Dietary Tocotrienols Reduce Concentrations of Plasma Cholesterol,

Apolipoprotein

B, Thromboxane. . . By Tocotrienols (Palmvitee)", Am. J. Clin.

Nutr.,

53, pp. 1021S-26S (1991); D. T. S. Tan et al., "The Effect Of **Palm Oil** Vitamin E Concentrate On The Serum And Lipoprotein Lipids In Humans", Am. J. Clin. Nutr., 53, pp. 1027S-30S (1991)). In. . .

DETD TRF Standard--A tocotrienol-rich fraction (TRF) obtained from **palm oil** (A. A. Qureshi et al. (1991), supra). The TRF Standard contains varying amounts of .alpha.-, .gamma.- and .delta.-tocotrienol and .alpha.-tocopherol. . .

DETD . . . milkweed, flax, sesame, rice bran, parboiled brown rice, brown rice flour, olives, vegetable oil distillant, fruit concentrate evaporate, barley bran, **palm oil**, wheat germ oil, rice bran oil, barley oil, **coconut oil**, **cottonseed oil**, **soybean oil**, other

cereal grains and other cereal grain oils, plant tissues, flowers, bushes (such as juniper), trees (such as pine and. . .

DETD Pharmaceutical compositions may take the form of tablets, capsules, **emulsions**, suspensions and powders for oral administration, sterile solutions or **emulsions** for parenteral administration,

sterile solutions for intravenous administration and gels, lotions and cremes for topical application. The pharmaceutical compositions may. . .

DETD . . . thereof, and a pharmaceutically acceptable carrier. Such carriers may be solid or liquid, such as, for example, cornstarch, lactose, sucrose, **olive oil or sesame oil**. If a solid carrier is used, the dosage forms may be tablets, capsules or lozenges. Liquid dosage forms include soft. . .

DETD . . . used in combination with bile acid sequestrants, such as Cholestyramine and Colestipol; fibric acid derivatives, such as, Clofibrate, Gamfibrozil, Bezafibrate, **Fenofibrate**, and Ciprofibrate; HMG-R inhibitors, such as Lovastatin, Mevastatin, Pravastatin, Simvastatin and SRI-62320; Probucol; Nicotinic Acid; its derivatives and conjugates, such. . .

DETD

| Ingredients | Weight (g) |
|-------------|------------|
|-------------|------------|

| | |
|-----------------------|-------|
| Corn (8.8% protein) | |
| | 615.0 |
| Soybean Meal | 335.0 |
| Corn Oil | 10.0 |
| Calcium Carbonate | |
| | 10.0 |
| Dicalcium Phosphate | |
| | 20.0 |
| Iodized Salt | 5.0 |
| Mineral Mixture.sup.a | |
| | 2.5 |
| Vitamin Mixture.sup.b | |
| | 2.5 |

.sup.a Mineral mixture contained per kg feed: zinc sulfate.H₂O. . .
DETD . . . of the chicken mash diet containing a 5% supplement of various oils. The control diet included a supplement of 5% **corn oil**. After 4 weeks, the birds were fasted for 36 hours and then refed for 48 hours prior to sacrifice (at. . .).

DETD

. . . Glucose

1)

Chick Diet + 5.0%

| | | |
|-------|------|------------|
| 185.1 | .+-. | 5.1.sup.A |
| 110.3 | .+-. | 4.95.sup.A |
| 61.9 | .+-. | 4.49.sup.A |
| 90.2 | .+-. | 2.17.sup.A |
| 124.6 | .+-. | 2.30.sup.A |

Corn Oil (CDC)

| | |
|---------|--------|
| (100.0) | .sup.2 |

2)

Chick Diet + 5.0%

| | | |
|-------|-------|------------|
| 129.7 | .+-. | 4.1.sup.B |
| 99.8 | .+-. | 3.57.sup.A |
| 27.9 | .+-. | 2.60.sup.B |
| 84.5 | . . . | |

DETD

. . . (nmoles/mg/min).sup.3

1)
Chick Diet + 5.0%
 185.1 .+- .4.12.sup.A
 110.3 .+- .4.95.sup.A
 61.9 .+- .1.49.sup.A
 344.3 .+- .1.49.sup.A
 0.855 .+- .0.084.sup.A

Corn Oil (CDCO)
 (100.0).sup.4
 (100.0).sup.4
 (100.0).sup.4
 (100.0).sup.4
 (100.0).sup.4

2)
Chick Diet + 5.0%
 184.7 .+- .6.50.sup.A
 109.6 .+- .2.83.sup.A
 61.7 .+- .1.71.sup.A
 339.3 .+- .19.7.sup.A
 0.837 .+- .0.081.sup.A

Corn Oil + Waxes;
 (99.8) (99.4) (99.7)
 (98.5) (97.9)

50 ppm

3)
Chick Diet + 5.0%
 173.8 .+- .7.31.sup.A
 106.2 .+- .4.69.sup.A
 58.1 .+- .1.77.sup.A
 317.1 .+- .14.4.sup.A,B
 0.846 .+- .0.072.sup.A

Corn Oil + Waxes;
 (93.9) (96.3) (93.9)
 (92.1) (98.9)

5,000 ppm

4)
Chick Diet + 5.0%
 165.9 .+- .4.90.sup.B
 108.5 .+- .4.68.sup.A
 57.9 .+- .1.48.sup.A
 304.5 .+- .14.4.sup.B
 0.902 .+- .0.080.sup.A

Corn Oil + Waxes;
 (89.6) (98.4) (93.5)
 (88.4) (105.5)

10,000 ppm

5)
Chick Diet + 5.0%
 134.8 .+- .3.82.sup.C
 104.3 .+- .3.99.sup.A
 25.9 .+- .1.02.sup.B
 276.0 .+- .17.4.sup.C
 1.068 .+- .0.047.sup.B

Corn Oil +
 (72.8) (94.6) (41.8)
 (80.2) (124.9)

Tocotrienol-Rich-
 Fraction; 50 ppm

6)
Chick Diet + 5.0%

180.2 .+- .6.01.sup.A
104.0 .+- .4.57.sup.A

DETD

(ng/ml)

1)

Chick Diet + 5.0%

61.4 .+- .2.4.sup.A
90.2 .+- .1.17.sup.A
124.6 .+- .2.3.sup.A
16.7 .+- .1.69.sup.A
7.2 .+- .0.48.sup.A

Corn Oil (CDCO)

(100.0).sup.3
(100.0).sup.3
(100.0).sup.3
(100.0).sup.3
(100.0).sup.3

2)

Chick Diet + 5.0%

62.5 .+- .1.9.sup.A
91.5 + 1.48.sup.A
126.7 .+- .2.1.sup.A
15.8 .+- .1.29.sup.A
7.5 .+- .0.42.sup.A

Corn Oil + Waxes;

(102.0).sup.3
(101.4).sup.3
(101.7).sup.3
(94.6).sup.3
(104.2).sup.3

50 ppm

3)

Chick Diet + 5.0%

63.6 .+- .2.8.sup.B
95.2 .+- .1.01.sup.A
123.9 .+- .1.52.sup.A
16.4 .+- .1.66.sup.A
7.4 .+- .0.36.sup.A

Corn oil + Waxes;

(103.8).sup.3
(105.5).sup.3
(99.4).sup.3
(98.2).sup.3
(102.8).sup.3

5,000 ppm

4)

Chick Diet + 5.0%;

60.4 .+- .1.9.sup.A
96.1 .+- .1.90.sup.A
124.3 .+- .1.18.sup.A
16.8 + 1.67.sup.A
7.4 .+- .0.87.sup.A

Corn oil + Waxes;

(98.5).sup..sup.3
(106.5).sup.3
(99.8).sup.3
(100.6).sup.3
(102.8).sup.3

10,000 ppm

5)
Chick Diet + 5.0%
68.5 .+- .2.1.sup.B
73.2 .+- .1.69.sup.B
86.4 .+- .1.55.sup.B
12.4 .+- .1.42.sup.B
5.7 .+- .0.64.sup.B

Corn oil +
(111.7).sup.3
(81.2).sup.3
(69.3).sup.3
(74.3).sup.3
(79.2).sup.3

Tocotrienol-Rich-
Fraction; 50 ppm

6)
Chick Diet + 5.0%
65.8 .+- .1.2.sup.B
89.5 + 1.21.sup.A

L6 ANSWER 3 OF 6 USPATFULL

AB Ergostanone derivatives substituted with disaccharides are cholesterol absorption inhibitors useful in the treatment of hypercholesterolemia and related disorders. These cholesterol absorption inhibitors may be employed alone or in combination with other cholesterol lowering agents.

AN 97:118019 USPATFULL
TI Steroidal glycosides as antihyperlipidemic agents
IN Kim, Dooseop, Westfield, NJ, United States
PA Merck & Co., Inc., Rahway, NJ, United States (U.S. corporation)
PI US 5698527 19971216 <--
AI US 1996-688582 19960730 (8)
DT Utility
FS Granted
EXNAM Primary Examiner: Owens, Amelia
LREP Quagliato, Carol S, Winokur, Melvin
CLMN Number of Claims: 13
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1307

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

PI US 5698527 19971216 <--

SUMM . . . lipid deposition in the rabbit aorta. Male New Zealand white rabbits are fed a diet containing 0.4% cholesterol and 5% peanut oil for 1 week (meal-fed once a day). After 1 week, the rabbits are dosed daily with the desired concentration of. . .

SUMM . . . forms as tablets, capsules (each including timed release and sustained release formulations), pills, powders, granules, elixirs, tinctures, suspensions, syrups and emulsions. Likewise, they may also be administered in intravenous (both bolus and infusion), intraperitoneal, subcutaneous or intramuscular form, all using forms.

SUMM . . . synthetase inhibitors (also known as squalene synthase inhibitors), acylcoenzyme A: cholesterol acyltransferase (ACAT) inhibitors; probucol; niacin; fibrates such as clofibrate, fenofibrate, and gemfibrozil; bile acid sequestrants; LDL (low density lipoprotein) receptor inducers; vitamin B_{sub}.6 (also known as pyridoxine) and the pharmaceutically. . .

SUMM . . . 1000 mg probucol, up to 2 g clofibrate, 0.5 to 8 g of niacin, 800 to 1500 mg gemfibrozil or **fenofibrate**, or 20 to 300 mg of an LDL receptor gene inducer.

L6 ANSWER 4 OF 6 USPATFULL

AB Therapeutic compositions comprising an effective amount of at least one carbonyl trapping agent alone or in combination with a therapeutically effective of a co-agent or medicament are disclosed. The compositions are used to treat a mammal suffering from a neurological disease characterized by covalent bond crosslinking between the nerve cells, other cellular structures and their intracellular and extracellular components, with disease induced carbonyl-containing aliphatic or aromatic hydrocarbons present in mammals.

AN 97:83944 USPATFULL

TI Methods of treating neurological diseases and etiologically related symptomatology using carbonyl trapping agents in combination with previously known medicaments

IN Shapiro, Howard K., 214 Price Ave. F32, Narberth, PA, United States 19072

PI US 5668117 19970916 <--

AI US 1993-62201 19930629 (8)

RLI Continuation-in-part of Ser. No. US 1993-26617, filed on 23 Feb 1993, now abandoned which is a continuation of Ser. No. US 1991-660561, filed on 22 Feb 1991, now abandoned

DT Utility

FS Granted

EXNAM Primary Examiner: Kight, John; Assistant Examiner: Leary, Louise

LREP Perrella, D. J.

CLMN Number of Claims: 29

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 3963

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

PI US 5668117 19970916 <--

SUMM . . . Grundy, 1990), bezafibrate (Olsson and Lang, 1978a; Olsson and Lang, 1978b; Zimmermann and coworkers, 1978; Monk and Todd, 1987) and **fenofibrate** (Elsom and coworkers, 1976; Wulfert and coworkers, 1976); metformin (Hermann, 1979); guar gum (Lalor and coworkers, 1990); 3-hydroxy-3-methylglutaryl-CoA reductase inhibitors. . .

SUMM . . . for patients suffering from these chronic, age-related diseases. Previously recognized drugs for treatment of atherosclerosis include hypolipidemic agents such as **fenofibrate** (Elsom and coworkers, 1976; Wulfert and coworkers, 1976), bezafibrate (Olsson and Lang, 1978a; Olsson and Lang, 1978b; Zimmermann and coworkers, . . .

SUMM bound . . . acetate, generating primary amine groups still covalently

to the polysaccharide. Chitosan has recognized uses in water treatment, in photographic **emulsions**, and in improving the durability of synthetic fabrics and fibers. The free amine groups in this substance also give it. . .

SUMM The ingredients as listed on the label are: "dicalcium phosphate, d-calcium pantothenate, pyridoxine hydrochloride, hydrogenated **cottonseed oil**, cellulose, niacinamide, rifoflavin, thiamine mono-nitrate, stearic acid, modified cellulose gum, magnesium stearate, silica, resin, gum acacia, hydroxypropylcellulose, rice bran, yeast,. . .

DETD **fenofibrate**, dosage range from 40 mg daily to 500 mg daily;

DETD **fenofibrate**, dosage range from 40 mg daily to 500 mg daily;

L6 ANSWER 5 OF 6 USPATFULL

AB There is provided a carrier for hydrophobic drugs, and pharmaceutical compositions based thereon, which carrier comprises a digestible oil and
 a pharmaceutically acceptable surfactant component for dispersing the oil in vivo upon administration of the carrier, which comprises a hydrophilic surfactant, said surfactant component being such as not to substantially inhibit the in vivo lipolysis of the digestible oil.
 AN 97:58921 USPATFULL
 TI Delivery systems for hydrophobic drugs
 IN Lacy, Jonathan Ernest, Swindon, United Kingdom
 Embleton, Jonathan Kenneth, Berkshire, United Kingdom
 PA R. P. Scherer Corporation, Troy, MI, United States (U.S. corporation)
 PI US 5645856 19970708 <--
 WO 9524893 19950921 <--
 AI US 1995-446874 19950606 (8)
 WO 1995-GB561 19950316
 19950606 PCT 371 date
 19950606 PCT 102(e) date
 PRAI GB 1994-5304 19940316
 DT Utility
 FS Granted
 EXNAM Primary Examiner: Page, Thurman K.; Assistant Examiner: Spear, James M.
 LREP Pearne, Gordon, McCoy & Granger LLP
 CLMN Number of Claims: 23
 ECL Exemplary Claim: 1
 DRWN 3 Drawing Figure(s); 3 Drawing Page(s)
 LN.CNT 1382
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.
 PI US 5645856 19970708 <--
 WO 9524893 19950921 <--
 SUMM . . . include a surfactant component. Lipophilic surfactants (i.e. HLB<10) are capable of promoting some emulsification of the oil but the resulting **emulsions** are normally too crude, in terms of size, to be useful. Hydrophilic surfactants (i.e. HLB>10) are much superior with respect to forming oil-in-water (o/w) **emulsions** and can be used to produce fine, uniform **emulsions** which are more likely to empty rapidly and uniformly from the stomach and coupled with a very large surface area. . .
 DRWD 6. **Castor oil ethoxylates** (low **ethoxylate** content, HLB<10) e.g.
 Etocas 5 (5 moles of ethylene oxide reacted with 1 mole of **castor oil**) Sandoxylate 5 (5 moles of ethylene oxide reacted with 1 mole of **castor oil**)
 DRWD 7. Acid and ester **ethoxylates**--formed by reacting ethylene oxide with fatty acids or glycerol esters of fatty acids (HLB<10) e.g. Crodet 04 (polyoxyethylene (4) lauric acid) Cithrol. . .
 DRWD . . . of natural or hydrogenated vegetable oil triglyceride and a polyalkylene polyol (HLB<10)
 e.g. abrafil M1944CS (polyoxyethylated apricot kernal oil) Labrafil M2125CS (polyoxyethylated corn oil) Gelucire 37/06 (polyoxyethylated hydrogenated oil)
 DRWD 2. Polyoxyethylene **sorbitan fatty acid** derivates e.g. Tween 20 (polyoxyethylene (20) monolaureate) Tween 80 (polyoxyethylene (20) monooleate) Crillet 4 (polyoxyethylene (20) monooleate) Montanox 40 (polyoxyethylene (20) monopalmitate)

- DRWD 3. Castor oil or hydrogenated castor oil
ethoxylates (HLB>10) e.g. _____ C
 remophor EL (polyoxyethylene (35) **castor oil**
)Cremophor RH40 (polyoxyethylene (40) hydrogenated
castor oil)Etocas 40 (polyoxyethylene (40)
castor oil)Nikkol HCO-60 (polyoxyethylene (60)
 hydrogenated **castor oil**
)
- DRWD 4. Fatty acid **ethoxylates** (HLB>10)
 e.g. _____ Myrj 45
 (polyoxyethylene
 (8) stearate)Tagat L (polyoxyethylene (30) monolaurate)Marlosol
 1820 (polyoxyethylene (20) stearate)Marlosol OL15 (polyoxyethylene (15)
 oleate)
- DRWD 5. Alcohol **ethoxylates** (HLB>10) e.g.
 Brij 96 (polyoxyethylene (10) oleyl ether)Volpo 015
 (polyoxyethylene (15) oleyl ether)Marlowet OA30 (polyoxyethylene (30)
 oleyl ether)Marlowet LMA20 (polyoxyethylene (20)). . .
- DRWD . . . oils which may be used include those containing saturated
 C.sub.6 -C.sub.12 fatty acids, for instance fractionated vegetable oils
 e.g. fractionated **coconut oils**. Specific examples of
 useful capric and/or caprylic triglyceride oils include: Miglyol 810,
 Miglyol 812, Neobee M5, Neobee O, Captex 300,. . .
- DRWD Lipid regulating agents: bezafibrate, clofibrate, **fenofibrate**,
 gemfibrozil, probucol.
- DRWD In the stomach the oil is physically emulsified with gastric juice to
 form an oil-in-water (o/w) **emulsion**. Hydrophobic drugs will
 reside predominantly within the dispersed (i.e. oil) phase of this
emulsion as either a solution or partial suspension.
- DRWD The o/w **emulsion** is not digested to any significant extent in
 the stomach with the result that the hydrophobic drug will enter the.
- DRWD . . . much higher solubilising power for hydrophobic drugs than pure
 bile salt micelles. This is illustrated with the hydrophobic
 antihyperlipoproteinemic drug **fenofibrate** which we have shown
 is >20 times more soluble in mixed micelles than simple bile salt
 micelles.
- DETD Effects of a Hydrophilic Surfactant on the Lipolysis Rate for
 Fractionated **Coconut Oil** (FCO) in the absence of a
 Lipophilic Surfactant
- DETD The drugs investigated using this method were: Carbamazepine,
 griseofulvin, **fenofibrate** and probucol.
- DETD Solubility (Relative to Buffer)
- Experiment
- | | Carbamazepine | Griseofulvin | Fenofibrate | Probucol |
|-----|---------------|--------------|--------------------|----------|
| i | 1 | 1 | 1 | 1* |
| ii | 1.1 | 4.6 | 38.5 | >71.0 |
| iii | 2.6 | 7.4 | 188.5 | >320.0 |
| iv | 2.7 | 6.6 | 930.0 | >77.0 |

*Buffer solubility of. . .

DETD Component mg/cap % w/w

Fractionated coconut oil

| | | |
|----------------|------|-------|
| | 190 | 17.19 |
| Imwitor 988 | 285 | 25.79 |
| Cremophor RH40 | 285 | 25.79 |
| Maisine 35-1 | 95 | 8.60 |
| Ethanol | 200 | 18.10 |
| Progesterone | 50 | 4.52 |
| TOTAL | 1105 | 100 |

DETD

| | |
|-----------------------|--------|
| Polysorbate 80 | |
| 275 mg | |
| Priolene | 275 mg |
| Soybean Oil | |
| 185 mg | |
| Triacetin | |
| 185 mg | |
| Fenofibrate | |
| 80 mg | |

DETD

| | |
|---------------------------------|--------|
| Cremophor RH40 | 300 mg |
| Fractionated Coconut Oil | |
| | 240 mg |
| Maisine | 200 mg |
| Imwitor 988 | 110 mg |
| Ethanol | 100 mg |
| Progesterone | 50 mg |

DETD

| | |
|---------------------------------|--------|
| Cremophor RH40 | 225 mg |
| Fractionated Coconut Oil | |
| | 315 mg |
| Crill 1 | 360 mg |
| Griseofulvin | 100 mg |

DETD

| | |
|-----------------------|--------|
| Polysorbate 80 | |
| 280 mg | |
| Soybean Oil | |
| 340 mg | |
| Priolene | 280 mg |
| Probucol | 100 mg |

DETD

| | |
|---------------------------------|--------|
| Labrasol | 330 mg |
| Fractionated Coconut Oil | |
| | 120 mg |
| Phenytoin | 50 mg |

DETD

| Component | Concentration (% w/w) |
|-----------|-----------------------|
|-----------|-----------------------|

| | |
|---------------------------------|----|
| Progesterone | 4 |
| Fractionated coconut oil | |
| | 16 |
| Cremophor RH40 | 28 |
| Lauroglycol | 37 |
| Ethanol | 15 |

| DETD | Component | Concentration (% w/w) |
|------|--------------------|-----------------------|
| | Progesterone | 4 |
| | Soybean oil | 16 |
| | Tween 80 | 20 |
| | Imwitor 988 | 45 |
| | Ethanol | 15 |

CLM What is claimed is:

5. A pharmaceutical composition according to claims 2, 3 or 4 wherein said hydrophilic surfactant component comprises a **castor oil** or hydrogenated castor **ethoxylate** having an HLB value greater than 10.
6. A pharmaceutical composition according to claim 5, wherein said hydrophilic surfactant component comprises a polyoxyethylene hydrogenated **castor oil**.

L6 ANSWER 6 OF 6 USPATFULL

AB The present invention relates to novel tocotrienols and tocotrienol-like

compounds displaying biological activity. The tocotrienols and tocotrienol-like compounds of this invention may be conveniently obtained from biological sources or by chemical synthesis and may be used in pharmaceutical compositions, foodstuffs and dietary supplements.

This invention also relates to the use of tocotrienols, tocotrienol-like

compounds, and mixtures thereof, as hypocholesterolemic, antithrombotic, antioxidantizing, antiatherogenic, antiinflammatory and immunoregulatory agents, or as agents useful to decrease lipoprotein (a) concentration in

the blood or to increase feed conversion efficiency.

AN 97:1493 USPATFULL

TI Tocotrienols and tocotrienol-like compounds and methods for their use

IN Lane, Ronald H., Phoenix, AZ, United States

Qureshi, Asaf A., Madison, WI, United States

Salser, Winston A., Pacific Palisades, CA, United States

PA Lipogenics, Inc., Scottsdale, AZ, United States (U.S. corporation)

PI US 5591772 19970107 <--

WO 9309777 19930527 <--

AI US 1994-244215 19940815 (8)

WO 1992-US10277 19921120

19940815 PCT 371 date

19940815 PCT 102(e) date

RLI Continuation-in-part of Ser. No. US 1991-796486, filed on 22 Nov 1991, now abandoned

DT Utility

FS Granted

EXNAM Primary Examiner: Raymond, Richard L.

LREP Lyon & Lyon

CLMN Number of Claims: 39

ECL Exemplary Claim: 1,2,3

DRWN 14 Drawing Figure(s); 13 Drawing Page(s)

LN.CNT 3224

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

PI US 5591772 19970107 <--
 WO 9309777 19930527 <--
 SUMM . . . ("T"). Tocotrienols and tocopherols occur naturally in small quantities in a wide variety of plant sources, such as rice bran, **palm oil** and barley (A. A. Qureshi et al., "Lowering of Serum Cholesterol in Hypercholesterolemic Humans by Tocotrienols (Palmvitee)", Am. J. Clin. . . .
 SUMM . . . al. (1986), Supra. Various human and animal studies have confirmed the impact of pure tocotrienols, isolated from barley, oats and **palm oil**, on cholesterol biosynthesis, specifically LDL-cholesterol (A. A. Qureshi et al., "Dietary Tocotrienols Reduce Concentrations of Plasma Cholesterol,
 Polipoprotein B, Thromboxane. . . Humans By Tocotrienols (Palmvitee)", Am. J. Clin. Nutr., 53, pp. 1021S-26S (1991); D.T.S. Tan et al , "The Effect Of **Palm Oil** Vitamin E Concentrate On The Serum And Lipoprotein Lipids In Humans", Am. J. Clin. Nutr., 53, pp. 1027S-30S (1991)). In. . .
 DETD TRF Standard--A tocotrienol-rich fraction (TRF) obtained from **palm oil** (A. A. Qureshi et al. (1991), supra). The TRF Standard contains varying amounts of .alpha.-, .gamma.- and .delta.-tocotrienol and .alpha.-tocopherol. . .
 DETD . . . milkweed, flax, sesame, rice bran, parboiled brown rice, brown rice flour, olives, vegetable oil distillant, fruit concentrate evaporate, barley bran, **palm oil**, wheat germ oil, rice bran oil, barley oil, **coconut oil**, **cottonseed oil**, **soybean oil**, other cereal grains and other cereal grain oils, plant tissues, flowers, bushes (such as juniper), trees (such as pine and. . .
 DETD Pharmaceutical compositions may take the form of tablets, capsules, **emulsions**, suspensions and powders for oral administration, sterile solutions or **emulsions** for parenteral administration, sterile solutions for intravenous administration and gels, lotions and cremes for topical application. The pharmaceutical compositions may. . .
 DETD . . . thereof, and a pharmaceutically acceptable carrier. Such carriers may be solid or liquid, such as, for example, cornstarch, lactose, sucrose, **olive oil** or **sesame oil**. If a solid carrier is used, the dosage forms may be tablets, capsules or lozenges. Liquid dosage forms include soft. . .
 DETD . . . used in combination with bile acid sequestrants, such as Cholestyramine and Colestipol; fibric acid derivatives, such as, Clofibrate, Gamfibrozil, Bezafibrate, **Fenofibrate**, and Ciprofibrate; HMG CoA inhibitors, such as Lovastatin, Mevastatin, Pravastatin, Simvastatin and SRI-62320; Probucol; Nicotinic Acid; its derivatives and conjugates, such. . .
 DETD

| Ingredients | Weight (g) |
|-----------------------|------------|
| Corn (8.8% protein) | 615.0 |
| Soybean Meal | 335.0 |
| Corn Oil | 10.0 |
| Calcium Carbonate | 10.0 |
| Dicalcium Phosphate | 20.0 |
| Iodized Salt | 5.0 |
| Mineral Mixture.sup.a | |

2.5
Vitamin Mixture.sup.b
2.5

.sup.1 Mineral mixture contained per kg feed: zinc sulfate.H.sub.2. . . .
DETD . . . of the chicken mash diet containing a 5% supplement of various
oils. The control diet included a supplement of 5% **corn**
oil. After 4 weeks, the birds were fasted for 36 hours and then
refed for 48 hours prior to sacrifice (at. . .).
DETD . . . Glucose

1)

Chick Diet + 5.0%
185.1 .+- .1.5.sup.A
110.3 .+- .4.95.sup.A
61.9 .+- .4.49.sup.A
90.2 .+- .2.17.sup.A
124.6 .+- .2.30.sup.A

Corn Oil (CDC)

(100.0).sup.2
(110.0).sup.2
(100.0).sup.2
(100.0).sup.2
(100.0).sup.2

2)

Chick Diet + 5.0%
129.7 .+- .4.1.sup.B
99.8 .+- .3.57.sup.A
27.9 .+- .2.60.sup.B
84.5. . .

DETD . . . (nmoles/mg/min).sup.3

1)

Chick Diet + 5.0%
185.1 .+- .4.12.sup.A
110.3 .+- .4.95.sup.A
61.9 .+- .1.49.sup.A
344.3 .+- .1.49.sup.A
0.855 .+- .0.084.sup.A

Corn Oil (CDCO)

(100.0).sup.4
(100.0).sup.4
(100.0).sup.4
(100.0).sup.4
(100.0).sup.4

2)

Chick Diet + 5.0%
184.7 .+- .6.50.sup.A
109.6 .+- .2.83.sup.A
61.7 .+- .1.71.sup.A
339.3 .+- .19.7.sup.A
0.837 .+- .0.081.sup.A

Corn Oil + Waxes;

(99.8) (99.4) (99.7) (98.5) (97.9)

50 ppm

3)

Chick Diet + 5.0%
173.8 .+- .7.31.sup.A
106.2 .+- .4.69.sup.A
58.1 .+- .1.77.sup.A

317.1 .+- .14.4.sup.A,B
0.846 .+- .0.072.sup.A

Corn Oil + Waxes;

(93.9) (96.3) (93.9) (92.1) (98.9)

5,000 ppm

4)

Chick Diet + 5.0%

165.9 .+- .4.90.sup.B

108.5 .+- .4.68.sup.A

57.9 .+- .1.48.sup.A

304.5 .+- .14.4.sup.B

0.902 .+- .0.080.sup.A

Corn Oil + Waxes;

(89.6) (98.4) (93.5) (88.4) (105.5)

10,000 ppm

5)

Chick Diet + 5.0%

134.8 .+- .3.82.sup.C

104.3 .+- .3.99.sup.A

25.9 .+- .1.02.sup.B

276.0 .+- .17.4.sup.C

1.068 .+- .0.047.sup.B

Corn Oil + Tocotrienol-Rich-

Fraction; 50 ppm

6)

Chick Diet + 5.0%

180.2 .+- .6.01.sup.A

104.0 .+- .4.57.sup.A

DETD

. . . (ng/ml)

1)

Chick Diet + 5.0%

61.4 .+- .2.4.sup.A

90.2 .+- .1.17.sup.A

124.6 .+- .2.3.sup.A

16.7 .+- .1.69.sup.A

7.2 .+- .0.48.sup.A

Corn Oil (CDCO)

(100.0).sup.3

(100.0).sup.3

(100.0).sup.3

(100.0).sup.3

(100.0).sup.3

2)

Chick Diet + 5.0%

62.5 .+- .1.9.sup.A

91.5 .+- .1.48.sup.A

126.7 .+- .2.1.sup.A

15.8 .+- .1.29.sup.A

7.5 .+- .0.42.sup.A

Corn Oil + Waxes;

(102.0).sup.3

(101.4).sup.3

(101.7).sup.3

(94.6).sup.3

(104.2).sup.3

50 ppm

3)

Chick Diet + 5.0%
63.6 .+- .2.8.sup.B
95.2 .+- .1.01.sup.A
123.9 .+- .1.52.sup.A
16.4 .+- .1.66.sup.A
7.4 .+- .0.36.sup.A

Corn Oil + Waxes;
(103.8).sup.3
(105.5).sup.3
(99.4).sup.3
(98.2).sup.3
(102.8).sup.3

5,000 ppm

4)
Chick Diet + 5.0%
60.4 .+- .1.9.sup.A
96.1 .+- .1.90.sup.A
124.3 .+- .1.18.sup.A
16.8 .+- .1.67.sup.A
7.4 .+- .0.87.sup.A

Corn Oil + Waxes;
(98.5).sup.3
(106.5).sup.3
(99.8).sup.3
(100.6).sup.3
(102.8).sup.3

10,000 ppm

5)
Chick Diet + 5.0%
68.5 .+- .2.1.sup.B
73.2 .+- .1.69.sup.B
86.4 .+- .1.55.sup.B
12.4 .+- .1.42.sup.B
5.7 .+- .0.64.sup.B

Corn Oil + (111.7).sup.3
(81.2).sup.3
(69.3).sup.3
(74.3).sup.3
(79.2).sup.3

Tocotrienol-Rich-
Fraction; 50 ppm

6)
Chick Diet + 5.0%
65.8 .+- .1.2.sup.B
89.5 .+- .1.21.sup.A